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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/034,621	12/21/2001	Walter Callen	DIVER1350-6	9848

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EXAMINER
HUTSON, RICHARD G

ART UNIT	PAPER NUMBER
1652	10

DATE MAILED: 08/20/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/034,621	CALLEN ET AL.	
	Examiner	Art Unit	
	Richard G Hutson	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 June 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17 and 28-38* is/are pending in the application.

4a) Of the above claim(s) *34,35 and 38* is/are withdrawn from consideration.

5)☒ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17,28-33,36 and 37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) *34,35,38* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6,9* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicants preliminary amendment of canceling claims 18-27, without prejudice, amending claims 1-17 and adding new claims 28-38, Paper No. 8, 6/2/2003, is acknowledged. Applicants amendment of claim 2 was not entered because the proposed amendment did not match claim 2. Claims 1-17 and 28-38 are still at issue and are present for examination.

Election/Restrictions

Applicant's election of Group I, Claims 1-17 in Paper No. 8 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Newly submitted claim 34, 35, and 38 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons:

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-17, drawn to an isolated nucleic acid encoding a polymerase, classified in class 435, subclass 194.

II. Claim 34 and 35, drawn to an method for amplifying a nucleic acid, classified in class 435, subclass 15

III. Claim 38, drawn to a method for identifying functional polypeptide fragments or variants, classified in class 435, subclass 15.

The inventions are distinct, each from the other because of the following reasons:

The elected invention of Group I drawn to nucleic acid is unrelated to the methods of Group II and Group III as they are neither used nor made by the method of Group II and Group III. It is noted that the method of Group III, claim 37, is the same as that of previous Group III and claim 27. Further, it is noted that the methods of Groups II and III are each methods of use of previous Group II drawn to a DNA polymerase.

Because these inventions are distinct for the reasons given above, have acquired a separate status in the art as shown by their different classification, and the literature and sequence searches required for each of the Groups are not required for another of the Groups, restriction for examination purposes as indicated is proper.

Accordingly, claim 34, 35, and 38 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claims 34, 35 and 38 withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Priority

Applicants statement on the first line of the specification that this application is a divisional of co-pending U.S. Patent Application Serial Number 09/656,309, filed September 6, 2000, which is a Continuation-in-Part application of co-pending U.S. Patent Application Serial Number 09/391,340, filed September 7, 1999, which is a divisional of U.S. Patent application Serial No. 08/907,166, filed August 6, 1997, now issued as U.S. Patent No. 5,948,666, is acknowledged. It is noted that application

09/391,740 has issued as U.S. Patent No. 6,492,511. It is suggested that applicants amend the specification to reflect this.

Information Disclosure Statement

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper."

Applicants filing of information disclosures,Paper No. 6, filed 10/2/2002, and Paper No. 9, filed 2/4/2003, are acknowledged. Those references considered have been initialed.

Specification

The disclosure is objected to because of the following informalities:

As suggested above, it is suggested that applicants amend the specification to reflect that application 09/391,740 has issued as U.S. Patent No. 6,492,511.

Appropriate correction is required.

Claim Objections

Claims 7-10 are objected to because of the following informalities:

Claim 1 recites "at least 70% identity to SEQ ID NO:1". It is suggested that this be amended to "at least 70% **sequence** identity to SEQ ID NO:1", for clarity purposes and to maintain consistency with other claims (i.e. claims 7-10) in the application.

Claim 37 recites "a baculovirus, a phase, a plasmid". It is suggested that applicants amend this to "a baculovirus, a phage, a plasmid". Unless applicants have some other expression vector in mind.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3, 4-6, 31, 32 and 37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 3 and 12 are indefinite in the recitation "sequences complementary thereto". Specifically it is indefinite in that it is unclear if when applicants recite "sequences complementary thereto " it is applicants intent that they mean sequences fully complementary to or sequences partially complementary thereto". While the specification on page 10, lines 22-30 discuss "complementary" with respect to nucleic acid primers, there is nothing to clarify applicants intended meaning with respect to partial or fully complementary. It is suggested that applicants amend the refereed to

recitation to "sequences fully complementary thereto", as this is how the recitation is interpreted for the sake of advancing prosecution.

Claims 4-6 are indefinite in the recitation of high stringency, moderate stringency and low stringency as the specification does not define what conditions constitute high, moderate and/or low stringency. While page 40 of the specification describe a variety of conditions which are intended to be high, moderate and/or low stringency, there is nothing to suggest that other conditions would not also be included within the scope of this term and in the art what is considered high, moderate and/or low stringency varies widely depending on the individual situation as well as the person making the determination. As such it is unclear how homologous to the sequence of a gene of SEQ ID NO:1, a sequence must be to be included within the scope of these claims.

Claims 31 and 32 are indefinite in that the recitations "wherein the polymerase activity comprises a 3'-5' exonuclease activity (claim 31) or lacks a 3'-5' exonuclease activity (claim 32)" are unclear. It is unclear how a "polymerase activity" can "comprise" or "lack" a 3'-5' exonuclease activity. For the sake of advancing prosecution, these claims are interpreted as "wherein the polymerase comprises a 3'-5' exonuclease activity (claim 31) or lacks a 3'-5' exonuclease activity (claim 32)".

Claim 33 is indefinite in that it is unclear and vague what is considered "high salinity conditions". Thus it is unclear what is considered to be encompassed by such conditions.

Claim 37 recites the limitation "the expression vector" of claim 1. There is insufficient antecedent basis for this limitation in the claim. For the purpose of

advancing prosecution the clam is interpreted as if it was drawn to the nucleic acid of claim 36.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 4-6, 7-11 and 12-17 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 4-6 are directed to all possible nucleic acids that hybridize under high to low stringency to the nucleic acid of claim 1 (i.e. a nucleic acid comprising a sequence having at least 70% identity to SEQ ID NO: 1 and encoding a polypeptide having polymerase activity). Claims 7-11 are directed to all possible nucleic acids having at least 70% identity to the nucleic acid of claim 1 (i.e. a nucleic acid comprising a sequence having at least 70% identity to SEQ ID NO: 1 and encoding a polypeptide having polymerase activity). Claims 12-15 are directed to all possible nucleic acids comprising at least 10 consecutive bases of SEQ ID NO: 1, or at least 10 consecutive bases of a sequence having at least 70% identity to SEQ ID NO: 1 and encoding a polypeptide with polymerase activity (claim 12) or those nucleic acids having at least 70%-90% identity to the nucleic acids of claim 12 (claims 13-15). Claims 16 and17 are directed to all possible nucleic acids encoding a polypeptide having a sequence

substantially identical thereto SEQ ID NO: 2 (claim 16) or all possible nucleic acids encoding a polypeptide comprising at least 10 consecutive amino acids of SEQ ID NO: 2 or sequences substantially identical thereto (claim 17).

The specification, however, only provides a single representative species isolated from *Pyrolobus fumarius*, having the sequence of SEQ ID NO: 1, encompassed by these claims. There is no disclosure of any particular structure to function/activity relationship in the single disclosed species. The specification also fails to describe additional representative species of these nucleic acids by any identifying structural characteristics or properties other than the relationship to the nucleic acid of claim 1 or SEQ ID NOs: 1 and 2, for which no predictability of function is apparent. Given this lack of additional representative species as encompassed by the claims, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 1-3, 4-6, 7-11, 12-17, 28-33, 36 and 37 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for nucleic acid comprising SEQ ID NO: 1 and encoding a polypeptide having polymerase activity, does not reasonably provide enablement for any nucleic acid comprising a mere 70% identity

to SEQ ID NO: 1 and encoding a polypeptide having polymerase activity, or any nucleic acid comprising a mere 10 consecutive bases of SEQ ID NO: 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 1-3, 28-33, 36 and 37 are so broad as to encompass any nucleic acid comprising a sequence having at least 70% identity to SEQ ID NO: 1 or sequences substantially identical thereto and encoding a polypeptide having polymerase activity (claims 1-3, 28, 30-33, 36 and 37), wherein said polypeptide has a polymerase activity at a temperature up to 150°C (claim 29). Claims 4-6 are so broad as to encompass any nucleic acid that hybridizes under high to low stringency to the nucleic acid of claim 1 (i.e. a nucleic acid comprising a sequence having at least 70% identity to SEQ ID NO: 1 and encoding a polypeptide having polymerase activity). Claims 7-11 are so broad as to encompass any nucleic acid having at least 70% identity to the nucleic acid of claim 1 (i.e. a nucleic acid comprising a sequence having at least 70% identity to SEQ ID NO: 1

and encoding a polypeptide having polymerase activity). Claims 12-15 are so broad as to encompass any nucleic acid comprising at least 10 consecutive bases of SEQ ID NO: 1, or at least 10 consecutive bases of a sequence having at least 70% identity to SEQ ID NO: 1 and encoding a polypeptide with polymerase activity (claim 12) or those nucleic acids having at least 70%-90% identity to the nucleic acids of claim 12 (claims 13-15). Claims 16 and17 are so broad as to encompass any nucleic acid encoding a polypeptide having a sequence substantially identical thereto SEQ ID NO: 2 (claim 16) or any nucleic acid encoding a polypeptide comprising at least 10 consecutive amino acids of SEQ ID NO: 2 or sequences substantially identical thereto (claim 17).

The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of nucleic acids broadly encompassed by the claims, including all nucleic acids comprising at least 10 consecutive bases of a sequence having at least 70% identity to SEQ ID NO: 1. Many of the claims rejected under this section of U.S.C. 112, first paragraph, place minor structural limitations on the claimed nucleic acids and many of the rejected claims place no functional limits on the claimed nucleic acids . Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited

to that nucleic acid comprising SEQ ID NO: 1 and encoding a polypeptide having polymerase activity.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass those nucleic acids comprising at mere 10 consecutive bases of a sequence having at least 70% identity to SEQ ID NO: 1, because the specification does not establish: (A) regions of the nucleic acid structure which may be modified without effecting the desired activity; (B) the general tolerance of the encompassed nucleic acids to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any nucleic acid residue of with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. Because of this lack of guidance, the extended experimentation that would be required to determine which substitutions would be acceptable to retain the desired activity/function and the fact that the relationship between the sequence of a peptide and its tertiary structure

(i.e. its activity) are not well understood and are not predictable (e.g., see Ngo et al. in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495, Ref: U, Form-892), it would require undue experimentation for one skilled in the art to arrive at the majority of those polypeptides of the claimed genus defined merely as all nucleic acids comprising at least 10 consecutive bases of a sequence having at least 70% identity to SEQ ID NO: 1.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of nucleic acid modifications of SEQ ID NO: 1. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 4-6, 7-11 and 12-17 are rejected under 35 U.S.C. 102(b) as being anticipated by Gelfand et al. (U.S. Patent No. 5,491,086, issued 2/13/1996).

Gelfand et al. teach a purified thermostable nucleic acid polymerase and DNA encoding said polymerase from *Pyrodictium* species. Gelfand specifically teach a nucleic acid from *P. occultum* (SEQ ID NO: 3) which is substantially identical to instantly disclosed SEQ ID NO: 1, as "substantially identical" is defined in the instant disclosure as two or more nucleic acid sequences that have at least 60% nucleotide identity (See page 14, lines 17-24 of specification) and SEQ ID NO: 3 disclosed by Gelfand is 66.5% identical to instantly disclosed SEQ ID NO: 1. Further the DNA taught by Gelfand et al. comprises many regions of at least 10 consecutive bases of sequence as set forth in SEQ ID NO: 1 and encodes a polypeptide comprising at least 10 consecutive amino acids of SEQ ID NO: 2.

Thus, Gelfand et al. anticipates claims 12-17 drawn to a recombinant nucleic acid, comprising at least 10 consecutive bases of SEQ ID NO: 1, or encoding a polypeptide comprising at least 10 consecutive amino acids of SEQ ID NO: 2. Gelfand et al. further anticipates claims 4-6 drawn to a recombinant nucleic acid that hybridizes to the nucleic acid comprising a sequence having at least 70% identity to SEQ ID NO: 1 and encoding a polymerase (claim 1) under conditions of high to low stringency. Gelfand et al. further anticipates claims 7-11 drawn to a recombinant nucleic acid having at least 70% to 95 % sequence identity to a nucleic acid having at least 70% sequence identity to SEQ ID NO: 1 and encoding a polymerase (claim 1).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-17, 28-33, 36 and 37 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-30 of U.S. Patent No. 5,948,666. An obvious type double patenting rejection is appropriate where conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g.., *In re* Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re* Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re* Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985).

Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1-13 of U.S. Patent No. 5,948,666, drawn to an isolated polynucleotide consisting of SEQ ID NO: 1, anticipate claims 1-17, 28-33, 36 and 37 of the instant application.

Remarks

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G Huston whose telephone number is (703) 308-0066. The examiner can normally be reached on 7:30 am to 4:00 pm, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (703) 308-3804. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Richard G Huston, Ph.D.
Primary Examiner
Art Unit 1652

rgh